IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE HONORABLE BOARD OF PATENT APPEALS AND INTERFERENCES

SUPPLEMENTAL APPEAL BRIEF
UNDER 37 C.F.R. §1.193(b)(2)(ii)

Appellant: Timo Nils-Erik LÖVGREN et al.
Serial Number: 08/487,623
Filed: June 7, 1995
Appeal No.:
Group Art Unit: 1645
Examiner: C. Spiegel
BIOSPECIFIC ASSAY METHOD

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Date: August 17, 1998

Atty. Docket No. TUR-026

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In re the application of

Timo Nils-Erik LÖVGREN et al.

Appln. S.N. 08/487,623

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For: BIOSPECIFIC ASSAY METHOD

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UNDER 37 C.F.R. §1.193(b)(2)(ii)

Assistant Commissioner
for Patents
Washington, D.C. 20231

August 17, 1998

Sir:

This is a supplemental appeal brief under 37 C.F.R. §1.193(b)(2)(ii). An appeal brief was filed in this application on December 8, 1997. Following the filing of the appeal brief, prosecution was reopened by the Primary Examiner in the Office Action dated March 17, 1998. Appellants have requested that the appeal be reinstated.

A petition for a two-month extension of the period for responding to the Action of March 17, 1998, is being filed concurrently herewith.

Items (1) to (7) of the brief filed December 8, 1998, have not changed except that issue (C) in item (6), "ISSUES", does not

include consideration of the Buechler et al. patent, U.S. Patent No. 5,089,391. The arguments below address the rejections made in the Office Action of March 17, 1998.

Prior to discussing the grounds of rejection in the Action, appellants have the following comments concerning the "BACKGROUND DISCUSSION" and the "THE INVENTION and THE PROBLEM" sections of the Action.

In the paragraph bridging pages 2 and 3 of the Action, the Examiner states that:

> "[i]n order to preserve signal strength which may otherwise be lost by washing steps or other additional liquid handling and/or dilution steps, it is the understanding of the Examiner, based upon the specification, that the signal from the reacted microparticles is individually measured (although more than one microparticle reading may be relied upon for improved reproducibility/reliability), and concentration is determined from a standard curve which correlates analyte concentration with signal strength from the same number of measured microparticles."

This understanding is not correct. First, the measurement of signal strength from an individual microparticle as recited in claim 13 on appeal is not made "to preserve signal strength which may otherwise be lost by washing steps or other additional liquid

handling and/or dilution steps." The measurement is made from an individual particle because according to the method of the present invention, "after the specific binding of the analyte in the sample to said predetermined number of uniformly sized particles, each individual particle emits a signal strength that corresponds to the analyte concentration in the sample." Measurement of the signal from one of the individual microparticles, therefore, provides an indication of the analyte concentration in the sample. The signal strength from more than one microparticle can be made to increase and ensure statistical reliability, but the measurement of the signal strength from all microparticles is not required or desired.

Second, contrary to the statement that the "signal from the reacted microparticles is individually measured", which suggests that the signal from all microparticles is measured, only the signal strength from the minimum number of microparticles required to ensure statistical reliability and, optimally, from one microparticle, is measured.

Third, the statement that the standard curve correlates the signal strength "from the same number of measured particles" is not

accurate because it suggests that the number of individual particles measured to determine analyte concentration is the same number that is used to determine the standard curve. Claim 13 specifically recites, however, that the standard curve is a mean of the signal strength of the predetermined particles, not the measured microparticles.

In the background discussion in the action, the Examiner also asserts that the record is confusing. The alleged confusion is not understood. Claim 13 recites measuring the signal strength from an individual microparticle. The wording "measuring the signal strength from an individual microparticle" does not require that each microparticle be measured, although the wording also does not preclude measuring the strength from more than one individual particle as desired. As noted above, by adjusting the relative amounts of sample and microparticles, the signal strength from an individual microparticle corresponds to the analyte concentration in a sample.

Under the heading "THE INVENTION and THE PROBLEM" the Examiner quotes the following sentence from the summary of the invention in the appeal brief filed December 8, 1997:

> The invention is the discovery that by appropriate control of the amount of microparticles and the amount of sample, the concentration of an analyte in a predetermined, clinically relevant range of analyte can be determined by measurement of the signal from a surface of a single microparticle. (sentence bridging pages 2 and 3).

She then states:

> "This begs the question as to whether or not analyte concentration **IS** determined by measurement of signal from a surface of a single microparticle. (Action, page 5, lines 6 and 7).

Appellants' statement is accurate and proper. The range of analyte <u>can</u> be determined from a single microparticle. If appellants had stated that the range of analyte <u>is</u> determined from one single microparticle, such statement would have indicated that their invention is restricted to the use of only one single microparticle for the measurement. This is not true because <u>one or more</u> individual microparticles can be used.

(8) ARGUMENT

A. The claims are definite within the meaning of the requirements of the second paragraph of 35 U.S.C. §112.

The claims stand rejected in the Action under the second paragraph of 35 U.S.C. §112 because it "is unclear as to what criteria are used to 'predetermine' the amount of microparticles and sample so as to correlate measurement of a single microparticle to analyte concentration." (Action, page 5, lines 13-15).

This statement has no meaning and is not a proper basis for rejecting the claims under the second paragraph of §112. Claim 13 precisely recites that the predetermined amount of sample and predetermined amount of microparticles are amounts such that, "after the specific binding of the analyte in the sample to said predetermined number of uniformly sized microparticles, each individual microparticle emits a signal strength that corresponds to the analyte concentration in the sample". Any means which enable a person of ordinary skill in the art to determine that, after the specific binding of the analyte in the sample to the microparticles, each individual microparticle emits a signal

strength that corresponds to the analyte concentration in the sample, can be used. As explained in the response filed December 10, 1996, to the Office Action dated June 10, 1996, the amount of sample and the number of microparticles are determined by experimentation using samples having a known concentration of analyte where the concentration is within a "typical" range. "Criteria", therefore, cannot and need not be recited in the claim.

It is also well established that the second paragraph of 35 U.S.C. §112 is a requirement for precision in claim language. A person of ordinary skill in the art must be able to determine from a reading of the claims in light of the specification disclosure, the subject matter covered by the claims. A person of ordinary skill in the art can readily determine whether the amount of sample and the number of microparticles used in a biospecific assay method as recited in the claims is such that each individual microparticle emits a signal strength that corresponds to the analyte concentration in a sample. The claims, therefore, are definite.

The second paragraph, 35 U.S.C. §112, ground of rejection is improper and should be reversed.

B. The claims are described in the specification disclosure in the manner required under the first paragraph of 35 U.S.C. §112.

The description requirement of the first paragraph of 35 U.S.C. §112 requires that a person of ordinary skill in the art recognize from the specification disclosure that applicants, i.e., the appellants, invented the subject matter that is being claimed. If the invention is described in the specification disclosure in terms commensurate in scope with those used in the claims, the description requirement is satisfied.

There is no requirement that a specification disclosure describe how a claimed invention differs from whatever the Examiner believes to be "routine optimization." Whether or not a claimed invention is "routine" optimization that will preclude patenting is a determination to be made under 35 U.S.C. §103(a) based on a comparison of a claimed invention with the prior art and is unrelated to the description requirement of §112.

The rejection under the first paragraph of 35 U.S.C. §112 is improper on its face and should be reversed.

C. The invention is not a "routine optimization" of the prior art and is otherwise not supported by the disclosures of the Soini et al., Ekins et al. and Bush et al. references, whether considered alone or in combination.

The Examiner's position as stated in the 35 U.S.C. §112, first paragraph, ground of rejection is that the predetermination of affinity microparticles and sample does not differ from what the Examiner has characterized as "routine optimization." It is well-established, however, that a suggestion to optimize must come from within the teachings of the prior art. The references cited in the 35 U.S.C. §103(a) ground of rejection do not support a conclusion that the present invention is a matter of optimization.

In the present invention, an amount of microparticles is used that is exactly known, i.e., predetermined. In the cited Soini et al. reference, on the other hand, it is not necessary to use an exactly known amount of microparticles. The only important condition is to use a sufficient amount of binding sites. It does not matter how great the excess of binding sites is. Soini et al. is representative of known immunoassays based on the use of a fixed sample volume in which the only criticalness is to use a sufficient

amount of binding sites for the analyte of the sample. In these immunoassays it has not been common to further "optimize" the amount of binding sites and the requirement for a sufficient amount of binding sites does not suggest decreasing the amount of microparticles as alleged by the Examiner. The present inventors were the first to carry out such modification. The invention, therefore, cannot be characterized as routine optimization.

Soini et al. also does not suggest the alleged "optimization." The reference discloses nothing concerning the amount of microparticles used in the method disclosed therein. Soini et al. discloses the use of the "smallest possible volume" of sample, but such disclosure is not equivalent to a suggestion to adjust the relative amount of sample and number of microparticles so that analyte concentration in a sample can be measured from the surface of a single microparticle.

Ekins et al. is alleged to disclose a generic optimization procedure. The Examiner fails, however, to explain the basis for such conclusion other than to suggest that appellants "see the entire article". (Action, page 8, lines 3-4). Nowhere does Ekins

et al. disclose that the procedure therein is applicable to a "normal" immunoassay using microparticles. The Ekins et al. invention is based on the theory of fractional occupancy when a very small and limited amount of antibody is used to bind a fraction of the analyte irrespective of the sample volume. The ratio between the total amount of antibody and the fraction of it that binds the antigen gives the answer, the amount of antigen measured.

It can be seen, therefore, that the method of Soini et al. (and that of the present invention) and that of the Ekins et al. reference are entirely different assay principles. In a fractional occupancy, the volume of sample is not specified. It is not clear, therefore, either why a person of ordinary skill in the art would have any motivation to combine the method of Ekins et al. with that of Soini et al. or what modification a person of ordinary skill in the art would make to the method of Soini et al. in view of the method of Ekins et al.

Moreover, even if it is assumed for the purpose of argument that the references can be combined, the rejection is not proper

because "prior art references in combination do not make an invention obvious unless something in the prior art references would suggest the advantage to be derived from combining their teachings." *In re Sernaker*, 217 USPQ 1, 6 (Fed. Cir. 1983).

The Bush et al. reference is cited as prior art only with respect to claim 7. The Bush et al. reference adds nothing, however, to the disclosures of the Soini et al. and Ekins et al. references. Claim 13 has been demonstrated to be patentable. Claim 7, therefore, is *prima facie* patentable.

The Soini et al. and Ekins et al. fail to support a case of *prima facie* obviousness under 35 U.S.C. §103(a) of claim 13 and the claims dependent thereon. Reversal of the 35 U.S.C. §103(a) rejection, therefore, is also in order.

In view of the foregoing arguments, appellant respectfully requests that the rejections of the Primary Examiner be reviewed and reversed.

Please charge any required fees or credit any overpayment to Deposit Account No. 11-1833.

Respectfully submitted,
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